Increased dengue transmissions in Singapore attributable to SARS-CoV-2 social distancing measures

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Article Summary

We used pre-post differences in dengue case counts and exploited heterogeneity in social distancing treatment effects among different age groups to identify the effects of distancing measures on dengue cases in Singapore. Social distancing policies caused an increased in over 37.2% of dengue cases from baseline.

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Abstract

Social distancing (SD) measures aimed at curbing the spread of SARS-CoV-2 remain an important public health intervention. Little is known about the collateral impact of reduced mobility on the risk of other communicable diseases. We used pre-post differences in dengue case counts and exploited heterogeneity in SD treatment effects among different age groups in Singapore to identify the spillover effects of SD measures. SD policy caused an increased in over 37.2% of dengue cases from baseline. Additional measures to pre-emptively mitigate the risk of other communicable diseases must be considered before the implementation/re-implementation of SARS-CoV-2 SD measures.

Keywords

Dengue; SARS-CoV-2; Interventions; Natural Experiment

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Background

An estimated 105 million dengue infections occur per year [1]. Primarily, the *Aedes aegypti* and *Ae. albopictus* vectors transmit the dengue virus. The combination of increasing human population connectivity, climate change and urbanisation within the region creates an ideal environment for dengue transmission and outbreaks to occur [2,3].

The unprecedented response to the ongoing COVID-19 pandemic has led to widespread social distancing (SD) and other non-pharmaceutical interventions. Population-wide implementation of SD has led to near complete lockdowns in most countries. However, despite the extant literature detailing how human mobility, importation, home-work infection patterns are key determinants of dengue epidemic potential, the effects of SD on vector-borne diseases such as dengue are not known. SD may bring hosts and vectors into closer proximity, if it results in social changes to the time spent at home, if the density of the anthropophilic *Ae. aegypti* is higher peridomestically.

In Singapore, the reduction of movements through workplace and school closures and cessation of mass gatherings were implemented and heavily enforced during SD policy. This has led to a large decrease in time spent in localities away from home (Appendix for summary) over a period of 2 to 3 months before gradual relaxation of measures. Most individuals of employment age in Singapore work in air-conditioned premises due to the highly developed economy [4]. The *Ae. aegypti* vector is a day biter with breeding most concentrated around residential areas [5]. Dengue infections at workplaces are rare at baseline, but the increase in dengue exposure risk due to increased time spent in residences due to SD is likely.

The near-complete coverage of SD policy across most age groups, regular and clear whole of government mass communication and heavy compliance through enforcement of said measures also greatly reduces policy leakage and non-compliance across the entire population. This provides a rare opportunity to identify the effects of shifting exposure patterns to residences on dengue transmissions by considering the implementation of SD policy as a natural experiment.

Methods

We obtained reported weekly case counts of dengue in Singapore by 5-year age bands from 2003 to 2020, where data was available till the 21th epidemiological week (EW) of 2020. All confirmed cases of dengue are legally required to be notified to the Ministry of Health for surveillance and control.

We controlled for the effects of weather on potential vector breeding, using weather data obtained from Meteorological Services Singapore. The measurements of each weather station for each day was averaged and temporally aggregated to the weekly frequency. Maximum and mean temperature, together with relative humidity, were used to represent thermal forcing and stress on vector population.

Intervention data for SD were obtained through the Ministry of Health, Singapore website. SD measures were implemented from 7 April 2020 to 1 June 2020, with varying degrees of strictness (Appendix for summary).

The primary goal of our analysis is to identify the effects of SD policy in Singapore on reported dengue case counts over time. In Singapore, SD policy led to a closure of around 95% of workplaces

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as well as all schools and recreational facilities [9]. The increase in time spent in residences and reduction in mobility patterns from SD policy would therefore most drastically affect individuals who are schooling or working prior to policy implementation. Treatment effects from SD policy can therefore be ascribed to those who are above 5 or below 65 years of age, which is around the retirement age in Singapore [4]. In Singapore, those who fall outside these bands mostly do not have drastic changes in mobility patterns from SD, as less than 50% of individuals below 5 attend child care centres for full-day programmes and less than 1% of individuals in retirement age reside in elderly care facilities [4]. A majority of individuals in the control group thus spends most of their time in residences or in the neighbourhood even before SD policy implementation.

Identification Strategy

The difference-in-difference (DiD) identification strategy was used to determine the causal effects of SD policy on dengue case counts over time. We took observations of reported dengue case counts within the 5–65 years old age bands during EWs when SD policy was implemented as the treatment group. Whereas all observations of reported dengue case counts within past EWs where SD policy was not implemented and for those in the below 5, above 70 age bands where SD policy was taken as the control group:

$$y_{i,t} = X\beta + I(\text{policy})_{i,t}\delta + \epsilon_{i,t}$$

where $y_{i,t}$ denotes the number of reported dengue case counts at time point t for the age band i. $I(\text{policy})_{i,t}$ is an indicator variable taking value 1 if SD policy effect was ascribed at that time point for that age band, 0 otherwise. The policy effect size, δ, is the primary estimand of interest. The error term $\epsilon_{i,t} \sim \mathrm{N}(0, \sigma^2)$ is normally distributed with constant variance σ^2. X is a matrix of controlling variables which include (1) time trend – to control for the temporal dependence of dengue case counts over time, as well as near-term trends in dengue transmission potential, (2) past EWs – to control for seasonality, (3) year fixed effects – to control for year specific risk, (4) maximum, mean temperature and relative humidity of up to 4 weeks lag – to control for thermal forcing and stress on vector population growth. The coefficient values for controlling variables are denoted β.

We built our DiD specification by sequentially adding confounders (1)–(4), to ensure robust identification of the policy effects, and to ensure that the policy effect of interest was not an artefact of other phenomena which affect dengue transmissions in the same period where SD policy was implemented. Other robustness checks to regression assumptions are reported in the appendix. In general, policy effects reported below are robust to relaxation changes in model specification.

No ethical approval was required for this study.

Results

[Insert Figure 1 Here]

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Figure 1: Reported dengue case counts for 2020 across epidemiological weeks for treatment (5 – 65 years old) and control (Below 5, Above 65 years old) groups.

SD causes increased incidence of dengue cases. The treatment effect ranges from 6.612 (Table 1 95% CI: 4.256–8.967) when controlling for EW as factors with year and age-group fixed effects, to 16.512 (Table 1 95% CI: 12.452–19.703) when controlling for EW as a linear trend. Controlling for all confounders, we estimate that there will be an increase in 9.873 cases (Table 1 95% CI: 7.528–12.219) per treatment group per week, this corresponds to around a 37.2% increase (95% CI: 19.9–49.8%) from expected baseline levels attributable to SD policy.

[Insert Table 1 Here]

Table 1 (1) – (6): Differences-in-differences specification estimated using ordinary least squares (1) without controlling for confounders (2) controlling for epidemiological week as a linear trend (3) controlling for epidemiological week as factors (4) controlling for epidemiological week as factors with year fixed effects (5) controlling for epidemiological week as factors with year and age-group fixed effects (6) controlling for epidemiological week as factors with 1-4 week lagged climate variables, year and age-group fixed effects. *denotes p-value<0.001

Discussion

Results indicate that implementation of SD is associated with an increase in the number of reported dengue cases in Singapore. One key pathway that may explain this result is the increased time spent in home addresses due to SD policy together with the propensity for dengue infections to surface at home rather than work addresses in Singapore [10]. Although workplace infections may surface, it was found that, in many areas, residences were the most common place of vector-borne disease infection, rather than workplaces [10]. Concentration of vector breeding sites around residential areas further compounds risk of transmission in these localities as compared to workplaces [5]. In conjunction with shifting work patterns into homes with naturally ventilated spaces which do not offer protection during the biting period in the day, these SD policy motivated pathways together converge risk factors of dengue transmission.

Cross immunity dynamics as a potential confounder

Cross immunity dynamics is well studied as a possible cause of dengue outbreaks in dengue endemic regions such as Singapore [11]. Virological surveillance in Singapore revealed an emergence of DENV-3 leading to co-dominance of DENV-2 and DENV-3 in 2020 in the same period SD policy occurred. While prior infection of individuals may have provided temporary/partial cross immunity, which thereby reduces the transmission potential of dengue in the community [12], this may have waned since the last outbreak in 2013. Antibody dependent enhancement, the posited pathway by which secondary infections of dengue become more severe and likely to be reported clinically, may have occurred in far more individuals, due to the emergence of DENV-3 and prior lack of exposure to this serotype in large proportions of the population.

Previous serotype switches to/from DENV-1 and DENV-2 have been linked to large outbreaks in Singapore have also suggested low population immunity to these strains [11]. Currently, immunity to DENV-3 even lower as it is not the predominant serotype in Singapore's dengue history until recently. These effects may have confounded the effect of SD on reported dengue cases in Singapore. The effects of serotype switching and other cross-immunity dynamics are however

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expressed in multi-annual cycles, which is unlikely to greatly bias policy effect estimates when policy is implemented only for the period of 2–3 months.

Implications for continued SD policy

Prior studies have showed that the likelihood of genetic diversity of dengue around home addresses to remain fixed in the absence of mobility and importation [13]. In conjunction with life-long immunity conferred after recovery from a specific serotype [12], the herd immunity within localities may increase, which will possibly lead to a decrease in the rise of dengue cases should SD policy persist.

Conversely, should SD policies ease and with dengue exposure patterns shifting back to the pre-SD policy regime, increases in mixing patterns away from home may lead to an increased risk of locality specific importation into residences. It is possible that an outbreak may be prolonged due to increased human mobility spatially spreading the high prevalence of virus. The impact of exiting from SD policy on dengue transmissions is however not quantified in this study and future work is necessary.

Of concern are also regions where SD policies have been instituted, relaxed and re-instituted such as Hong Kong, several states in the United States and China. Similar policy behaviour has not been observed in dengue hyper-endemic regions such as Singapore and Malaysia, but the effects of multiple entry and exits from SD policy on dengue transmissions are also not known. It is likely that SD policy institution, relaxation and re-institution regimes may amplify, mix then seed and amplify new areas of vector-borne disease transmission and should SD policy be re-instituted, vector control in residential areas should to pre-emptively employed to mitigate the transmission of dengue.

Implications for other vector-borne diseases

The efficacy of SD policy as a public health intervention for reducing the onward spread of respiratory diseases is well known as it reduces human contact by increasing time spent in residences. Increase in time spent in residences during the day and thus their exposure to vectors can likewise influence the transmission pattern of vector-borne diseases–but in an opposing direction. Increasing time spent at a locality elevates transmission risk of vector-borne diseases despite of vector density [14].

Prior studies have shown that the transmission risk of vector-borne diseases could be higher at home and in one's neighbourhood [15]. The highly urban environment of Singapore only allows identification of SD policy effects on reported dengue case counts, as other vector-borne diseases are not widespread. It is of interest to generalize the natural experiment design of SD on other vector-borne diseases as the transmission patterns of malaria are vastly different, in terms of vector breeding behaviour and viral dynamics. The differences in habitats for the respective vectors may result in differences in exposure risk before and after distancing policies.

The indirect effects of SARS-CoV-2 non-pharmaceutical interventions beyond that of SARS-CoV-2 transmissions need to be urgently quantified. This study reveals that SD policy has led to a sharp increase in dengue incidence in Singapore. Additional measures to pre-emptively mitigate the risk of other communicable diseases such as dengue must be considered during the implementation of SD measures.

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Notes

Contributors

LJT designed the study, conducted the analysis, validated the analysis. LJT, LCZX, ECSL wrote the manuscript. JO and JA collected the data. JO, JA and NLC conceptualized the study. ARC, NLC, BSD, JO, JA critically revised the manuscript.

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Conflict of Interest Statement

None declared for all authors.

Patient consent for publication

Not required.

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Dependent Variable: Weekly Reported Cases						
	(1)	(2)	(3)	(4)	(5)	(6)
Treatment Effect (δ)	15.865*	16.512*	15.692*	8.785*	6.612*	9.873*
Lower Bound (95% CI)	12.761	12.452	12.452	5.456	4.256	7.528
Upper Bound (95% CI)	18.969	19.703	18.932	12.115	8.967	12.219
Observations	2,776	2,776	2,776	2,776	2,776	2,776

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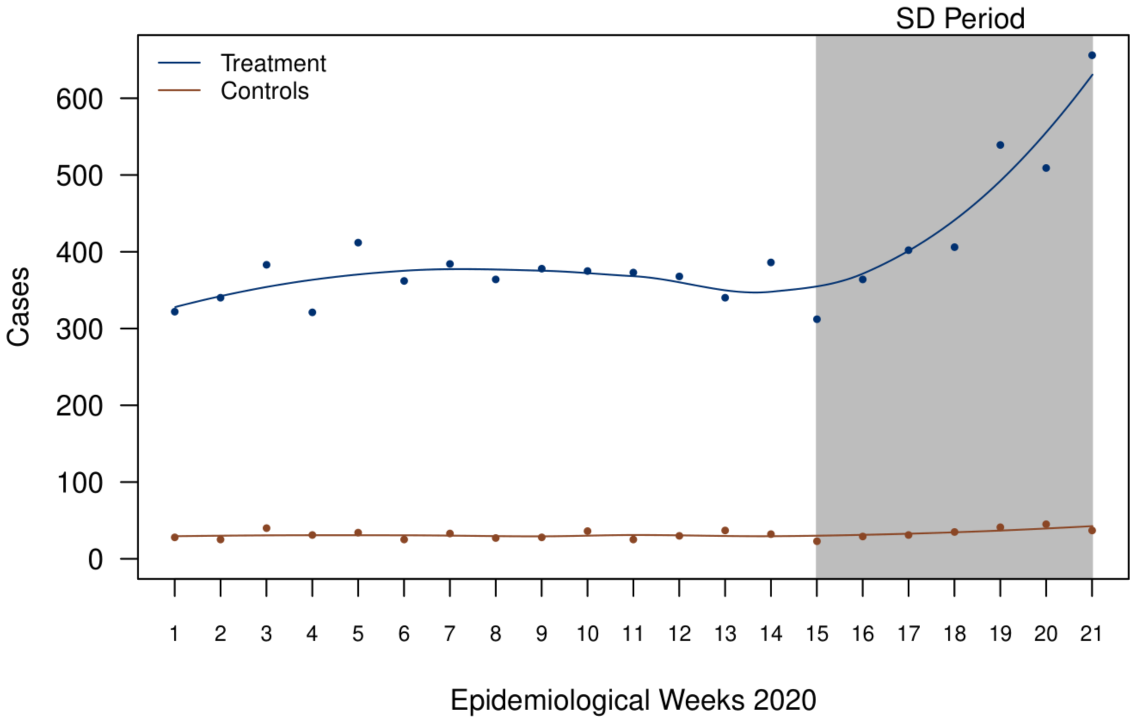
Figure 1



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